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COMMUNICATIONS

THE CHI-SQUARE TEST OF SIGNIFICANCE APPLIED TO A SERIES OF INTRA-CAPSULAR CATARACT EXTRACTIONS

BY

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GLASGOW

THE object of this paper is to extract information from a small series of intra-capsular cataract operations carried out upon hospital and private patients. The majority of ophthalmic surgeons in this country have to form their views either from a limited experience or else depend for their judgments upon authority at second hand. As clinical opinion is frequently based upon small numbers it seems desirable that an attempt should be made to weigh the probabilities. It is not necessary to know anything about the inner workings of a watch in order to tell the time of day and similarly we may employ complex statistical tests to control our clinical enthusiasms without pretending to be statisticians.

The intra-capsular operation was considered to be a suitable one in 88 out of 122 consecutive patients. The final decision as to the type of operation was not made until the section was completed. All the patients were in danger of having the operation performed and the reasons for rejection were those commonly described by other writers, inadequate control of the eye, insufficient working room for the intra-capsular forceps, too small a section, insufficient

dilatation of the pupil and so on. Any patient into whose eye intra-capsular forceps were inserted is classified as an intra-capsular extraction. This definition is used because it is in the manoeuvring of the forceps that the principal danger of the operation lies. The method employed was essentially that described by Sinclair (1932), and his single action forceps were used in most of the cases. A pair modified to my own design were found to have no advantages. The large majority of the operations were done without a skilled assistant and a conjunctival suture was used only on a few occasions.

There were 49 men and 73 women in the series, and it may be asked if this ratio does not show an excess of women. The mean age of the patients of both sexes was practically 65 years, with a standard deviation of 8 years. From the 1931 census figures for the West of Scotland the expected proportion in the age groups concerned was estimated to be 57·54 men and 64·46 women. From these figures it can be calculated whether the observed ratio differs from the expected one to a greater degree than might arise by chance. One method of doing this is shown in Table I.

TABLE I

Observed and Expected Sex Incidence

	Expected (m)	Observed (x)	Difference (x-m)	$\Sigma \frac{(x-m)^2}{m}$
Men ...	57·54	49	−8·54	1·2675
Women ...	64·46	73	+8·54	1·1278
Total ...	122	122		$\chi^2 = 2·3953$

The sum of the right hand column gives the value of a statistic known as chi-square (χ^2). As there is only one possible way of distributing the data there is only one degree of freedom (n). The probability (P) is obtained from a table showing the distribution of χ^2 for one degree of freedom and it is found to lie between 0·10 and 0·20. This test of significance has been elaborated for small samples by Professor R. A. Fisher although the distribution of χ^2 was established by Karl Pearson in 1900 (Fisher, 1938). The exact relationship between the χ^2 value and the probability (P) is an extremely complex one, but Fisher's table is suitable for the type of problem which arises in clinical work and is readily available (Mainland, 1938, Hill, 1939). The level of 0·05 or 5 per cent. is the usual dividing line which is made between events which are likely to have arisen by chance and those which are unlikely. In this case the result is above this conventional level and we may say that the observed figures do not show a significant excess of women. At the same time the probability is sufficiently low to arouse doubt, and on finer grouping of the material it was found that one hospital at one

period did in fact show a figure of 0·05 compared with 0·30 to 0·40 in the others. With the combined figures the higher probabilities were reduced and the figure 0·10 emerged.

It may be asked if the ratio of intra-capsular operations to other methods in hospital patients is no different from that in private patients. Such a proposition is called a null hypothesis and the object of the χ^2 test is to disprove it. The observed and expected ratios are shown in Table II, and it is quite obvious that the hypothesis is not disproved. The expected figures are calculated from the marginal totals. Only one cell requires to be filled by this

TABLE II

Distribution of hospital and private patients relative to the type of operation

	Observed				Expected		
	Intra-capsular	Other methods			Intra-capsular	Other methods	
Hospital	70	28	98	Hospital	70·69	27·31	98
Private	18	6	24	Private	17·31	6·69	24
	88	34	122		88	34	122

$\chi^2 = 0{\cdot}1223$ (Yates Correction 0·0091)
$n = 1$ $P = 0{\cdot}90$

means because the other three can be found by subtraction. There is therefore only one degree of freedom. In a 2×2 table such as this, where the expected number in any cell is five or less, a slightly different method of calculation is advisable, known as Yates' correction for continuity (Fisher, 1938). The χ^2 value by the ordinary method is 0·1223, and with Yates' correction it is 0·0091. This makes it highly probable that the hypothesis is true.

By constructing similar tables from the data it can be shown that there was no significant difference in the treatment between right and left eyes ($\chi^2=0.1284$ and $P=0{\cdot}70$) and that the sexes were treated alike with regard to the type of operation performed ($\chi^2=1{\cdot}3352$ and $P=0{\cdot}25$).

The vision recorded in all the intra-capsular patients is shown in Table III, and by arranging the data in age groups a form of correlation table is made. The visual acuity was entered in the cell appropriate to the last completed test line, thus 6/12 partly was classified as 6/18. The null hypothesis that there is no difference in the visual result between patients 64 years and under and those 65 years and over can be tested by re-grouping the material. This must be done because the test for significance becomes excessively complicated if any of the cells have small expectations. The

TABLE III

Visual results and age distribution

Vision	6/6	6/9	6/12	6/18	6/24	6/36	6/60	Bad	Total
AGE :									
59 and under ...	17	3	1	1	2	0	0	0	24
60-64	10	0	2	1	0	0	1	1	15
65-69	10	7	5	1	1	0	0	1	25
70 and over ...	1	10	4	4	2	0	1	2	24
TOTAL	38	20	12	7	5	0	2	4	88

TABLE IV

Grouped visual results and age

Observed

	6/6	6/9	6/12 & 6/18	6/24 & worse	
64 and under	27	3	5	4	39
65 and over	11	17	14	7	49
	38	20	19	11	88

Expected

	6/6	6/9	6/12 & 6/18	6/24 & worse	
64 and under	16·84	8·86	8·42	4·88	39
65 and over	21·16	11·14	10·58	6·12	49
	38	20	19	11	88

Contributions to χ^2

64 and under	6·0498	3·8757	1·3891	0·1585
65 and over	4·8784	3·0825	1·1055	0·1265

$\chi^2 = 20{\cdot}666$ $\quad n = 3$ $\quad P =$ less than 0·01

observed and expected figures with the contributions made to the total χ^2 from each cell is shown in Table IV. In this test three expected figures have to be calculated before the remaining cells can be filled in by subtraction from the marginal totals. There are therefore three degrees of freedom. With the grouping employed the χ^2 value is very high and the probability (P) that the visual result is unaffected by the age of the patient is extremely unlikely. This highly significant result from the test must be interpreted in

the light of the clinical facts and it raises the question whether we are justified in expecting our elderly patients to reach a standard of 6/6. The highest contributions to the total χ^2 are made by the 6/6 and 6/9 cells; there are too many younger patients with 6/6 and too few with 6/9. If these two cells are combined in both age groups the number of degrees of freedom becomes 2, $\chi^2=4{\cdot}0714$ and P. rises to 0·10 which is above the conventional level. This does not prove that no real difference is present with the data arranged in this way, but the null hypothesis is not disproved.

The null hypothesis that there is no difference between the five year age group distribution and vision of 6/9 or better and 6/12 or worse can be tested. The distribution is shown in Table V. The χ^2 value is 7·600, n=3 and P=0·05. This is at the level of significance and it is open to the observer to make what interpretation he chooses. I am indebted to Professor Fisher for the remainder of this paragraph. He pointed out to me that confidence in the reality of the effect of age is strengthened by the fact that the results in the four age groups fall out consistently in order of age, the contrast being greatest between the oldest and the youngest groups. One way of allowing this fact to weigh with the test is to consider only the 2×2 table supplied by the extreme classes in Table V, the youngest 20 and 4 and the oldest 11 and 13. Here with only one degree of freedom $\chi^2=7{\cdot}38$ showing that nearly all the heterogeneity observed among the four age groups is due to the contrast between the youngest and the oldest. With Yates' correction $\chi^2=5{\cdot}8$, so that P is well below 2 per cent.

TABLE V

Grouped visual results and age

	Observed		Expected		Contribution to χ^2	
	6/6-6/9	6/12 & worse	6/6-6/9	6/12 & worse		
59 and under	20	4	15·82	8·18	1·105	2·135
60-64 ...	10	5	9·88	5·12	0·001	0·003
65-69 ...	17	8	16·48	8·52	0·016	0·031
70 and over	11	13	15·82	8·18	1·468	2·840
Total ...	58	30	58	30		

$\chi^2 = 7{\cdot}600 \quad n = 3 \quad P = 0{\cdot}05$

Considered in conjunction with Table IV, I am of the opinion that a real difference is present. If the data are arranged in age groups as in Table V with the 6/6 patients tested against those

with 6/9 or worse, a result similar to that in Table IV is obtained with $\chi^2=27{\cdot}259$, n=3 and P very low, disproving the null hypothesis.

In 52 of the 88 patients the lens was removed completely intact. In 36 the capsule was ruptured either deliberately or by the forceps, the lens parting company involuntarily. The series was carried out with certain basic prejudices against the procedure and at a time when my operative work was limited. Feelings akin to those of a small boy stealing apples from an orchard tended to make delivery more rapid than was desirable and led to frequent rupture of the capsule at the final stage. This happened evenly throughout the series and in all the age groups (Table VI, A and B). In the latter group $\chi^2=2{\cdot}2439$, n=3 and P=0·50 and if the two younger and two older age groups are combined into a 2×2 table it becomes highly improbable that there is any difference between the ratios, the χ^2 value is lowered to 0·00392 and P=0·95. This technical failure appears to affect the visual result (Table VII) and by the test a significant difference is shown to be present ($\chi^2=8{\cdot}9765$, n=3 and P=0·02). This supports those who stress the superior visual results in successful intra-capsular extraction. It would appear that if the operation is confined to patients under 65 the better results are attributable to age rather than to the technique.

For purposes of comparison a series of fifty cataract extractions was compiled where the object was to carry out a simple extraction with a peripheral iridectomy followed by an early capsulotomy. The mean age of the series was 66·8 with a standard deviation of 7·5 years. The 34 patients of the original series could not be used as

TABLE VI

Intact and ruptured capsule

A — Serial distribution

Serial No.	Intact	Ruptured	
1—22 ...	14	8	
23—44 ...	13	9	
45—66 ...	13	9	
67—88 ...	12	10	
Totals ...	52	36	88

χ^2 value very low

B — Age distribution

	Intact	Ruptured	
Under 59	12	12	24
60—64 ...	11	4	15
65—69 ...	14	11	25
Over 70 ...	15	9	24
	52	36	88

$\chi^2 = 2{\cdot}2439$
n = 3
P = 0·50

TABLE VII

Effect of rupture of the capsule upon visual acuity

Observed

	6/6	6/9	6/12	6/18 & worse	
Intact	27	10	9	6	52
Ruptured ...	11	10	3	12	36
Totals	38	20	12	18	88

Expected

	6/6	6/9	6/12	6/18 & worse	
Intact	22·5	11·8	7·1	10·6	52
Ruptured ...	15·5	8·2	4·9	7·4	36
Total	38	20	12	18	88

$\chi^2 = 8{\cdot}9765 \quad n = 3 \quad P = 0{\cdot}02$

a basis of comparison because they were subjected to obvious selection. The observed differences and the χ^2 values are shown in Table VIII. The successful intra-capsular cases are just significantly better than the extra-capsular. There is no significant

TABLE VIII

Intra-capsular extraction compared with simple extraction with peripheral iridectomy

Lens delivered intact

	6/6	6/9	6/12	6/18 & worse	
Intra-capsular ...	27	10	9	6	52
Extra-capsular ...	14	16	7	13	50
Total	41	26	16	19	102

$\chi^2 = 8{\cdot}3014 \quad n = 3 \quad P = \text{under } 0{\cdot}05$

Rupture of lens capsule

	6/6	6/9	6/12	6/18 & worse	
Intra-capsular ...	11	10	3	12	36
Extra-capsular ...	14	16	7	13	50
Total	25	26	10	25	86

$\chi^2 = 1{\cdot}1637 \quad n = 3 \quad P = 0{\cdot}65$

difference between the ruptured capsule group and the extra-capsular operation. There is no reason to suppose that the two series did not come from a universe represented by the marginal totals. This conclusion is of some importance because it shows that if the operation was not technically successful the patients in my hands did not have a result any worse than those not exposed to the risks of intra-capsular extraction.

A matter of interest arises concerning operation upon the second eye. On eight occasions in this series one eye was done by the intra-capsular method and the other with a simple extraction with peripheral iridectomy in view. These cases are shown in Table IX. It is obvious that by this method it is possible to stabilise many

TABLE IX

Sex, age, and visual result in patients operated upon by both methods

No.	Sex	Age	Intra-capsular operation		Extra-capsular operation	
1.	M	52	R.E.	6/6	L.E.	6/6
2.	F	63	L.E.	6/6	R.E.	6/6
3.	M	64	L.E.	6/6	R.E.	6/6
4.	M	60	R.E.	6/6	L.E.	6/9
5.	F	60	R.E.	6/6	L.E.	6/9
6.	M	62	L.E.	6/9	R.E.	6/9
7.	F	65	R.E.	6 6	L.E.	6/12*
8.	F	62	L.E.	6/6	R.E.	6/18*

(*Patients 7 and 8 declined to have a capsulotomy performed.)

random factors which may affect the ultimate result and it appears to be the most likely way of forming an opinion as to the ultimate results over a period of years. It will be observed that two patients were unwilling to submit to a capsulotomy. They were quite happy with reversible glasses which they seldom altered. It is in this matter of prognosis after the operation that our knowledge appears to be most defective. Personally I would prefer to have an intra-capsular extraction performed upon one eye and an extra-capsular performed upon the other.

An account of adventures with individual cases is deliberately omitted because if complications had led to frequent disaster the results would have appeared in the tables. This has not occurred. In 2 out of the 88 patients I regret that the procedure was attempted. The operation is not one which should be attempted without meticulous attention to the detail described by such masters of the technique as Dr. A. H. H. Sinclair.

Summary

In a series of 122 senile cataract extractions the intra-capsular method was considered to be suitable in 88. The results have been treated statistically by the χ^2 test of significance. The sex ratio observed, the treatment of hospital and private patients, the treatment of right and left eyes and of the sexes have all been considered. A better visual result was found where the lens was removed intact within its capsule than in those cases where the capsule ruptured. Rupture of the capsule occurred evenly throughout the series and in all the age groups. Evidence is presented to show that the better visual results tend to occur below rather than over the age of 65, and that this is not necessarily attributable to the type of operation. Comparison is made with fifty patients in whom the operation intended was a simple extraction with a peripheral iridectomy followed by early capsulotomy. The intact intra-capsular cases gave the better visual result and those which ruptured did not differ significantly from the control group. In eight patients the two eyes were submitted to the different operations.

I have great pleasure in acknowledging to Dr. A. H. H. Sinclair the great help and encouragement which he has always given to me and I am indebted to Dr. John Gilchrist for permission to operate upon many cases primarily under his care.

The design of this paper is intended to show an application to clinical problems of the methods so ably advocated by Professor R. A. Fisher. Although he is not responsible for the accuracy of the calculations I am obviously deeply in his debt both for the method of approach and for his kindly criticism.

REFERENCES

1. FISHER, R. A.—The Design of Experiments. Second Edition, Edinburgh, 1937.
2. ——— Statistical Methods for Research Workers. Seventh Edition, Edinburgh, 1938.
3. HILL, A. BRADFORD.—Principles of Medical Statistics, Second Edition, London, 1939.
4. MAINLAND, DONALD.—The Treatment of Clinical and Laboratory Data, Edinburgh, 1938.
5. SINCLAIR, A. H. H.—*Trans. Ophthal. Soc. U.K.*, Vol. LII, 1932.

EXPERIMENTAL PIGMENTARY DEGENERATION OF THE RETINA BY SODIUM IODATE

BY

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SEPTOJOD,* which appears to have been introduced in 1920, has been used widely in German-speaking countries for septic conditions on the assumption that nascent iodine is liberated by this preparation in the presence of septic material. It has been especially popular in the treatment of puerperal sepsis.

In 1926, Schimmel and Riehm reported two cases of blindness following the intravenous injection of 150 c.c. septojod in patients with puerperal septicaemia. The blindness came on within twenty-four hours, whilst the fundi showed no abnormality; within the course of a few days oedema of the macular region set in to be followed by diffuse pigmentary changes all over the fundus, reminiscent of retinitis pigmentosa. In the same year, Scheerer reported a similar case, describing the fundus changes fully and regarding the condition as an acute tapeto-retinal degeneration. Further cases have been reported by Riehm (1927), Roggenkämper (1927), von Bunau (1929), Sallmann (1933), and Ohm (1934). Roggenkämper's patient had undergone an operation for varicose veins and the track left by the excised veins had been washed out with 380 c.c. of septojod; Ohm's patient had 150 c.c. injected in a ligated saphenous vein; Sallmann's patient, who suffered from tuberculous peritonitis, had undergone appendicectomy and the abdominal cavity had been flushed with 300 c.c. Pregl's solution, whilst the remaining cases—those of Riehm and von Bunau—were like the first three, cases of puerperal septicaemia. Ophthalmoscopically the patients all showed very similar appearances; a good coloured drawing is given by Riehm (1929). Variable field defects are reported and end results, varying from little recovery to practically complete recovery of vision, are noted. As to aetiology the later cases negative the suggestion made by Scheerer on the early cases, *viz.*, that the retina is affected by septojod only in cases of puerperal sepsis with its preceding loss of blood, and possible damage to the liver from chloroform.

* A German iodine preparation, the exact composition of which is a trade secret, is said to contain sodium hypoidide and sodium hypoiodate. According to Fernau, Pregl's solution (the basis of septojod which is said to be this solution ten times concentrated) contains iodide, hypoiodate, bicarbonate and chloride all as sodium salts and also free iodine. Gehr's Codex 1937 gives it as consisting of iodine, hypoiodide, iodate and a small quantity of free iodine.

The toxic component of septojod.—In reporting the first two cases (Schimmel and Riehm) Riehm gave experimental evidence to implicate septojod; in 18 rabbits 2·5—5·0 c.c. septojod per kilo injected intravenously produced an ophthalmoscopic picture similar to that they had observed clinically. In albino rabbits no tangible ophthalmoscopic changes were found. These findings are constant and have been confirmed by all the subsequent observers who have dealt with the experimental aspect of the subject. Sallmann investigated experimentally the toxic action of iodine, sodium iodide and sodium hypoiodate and concluded that it was the hypoiodate component of septojod which was responsible for the retinal degeneration, for ophthalmoscopically and histologically it gave regularly the same appearances as are given by septojod degeneration. Sodium hypochloride and sodium hypobromide could not be injected in corresponding quantities as they are highly irritating, and in the concentrations used gave no ophthalmoscopic changes, though the neuro-epithelium showed histological damage. Vito (1935), impressed by the fact that hypoiodate is an unstable compound, becoming readily converted into iodate on exposure to air, light, changes in temperature, and in acid media, attempted to obtain retinal degeneration by the action of sodium iodate alone. This he achieved in rabbits by injecting [?intravenously] ½—1 c.c. per kilo of 4·52 per cent. sodium iodate daily for 10-15 days. Fundus changes appeared early. Kalt (1937) confirmed these observations, but used the subcutaneous route, injecting 1 c.c. of 4 per cent. solution per kilo under the abdominal skin, and repeating it every second day, giving twenty to thirty injections.

Lesions in tissues other than the retina.—Riehm, Sallmann and Vito, all reported that no damage to other tissues could be detected in pigmentary retinal degeneration produced by septojod or by sodium hypoiodate and sodium iodate. Umadzume (1929) appears to have noted lesions in the liver, as also—in contrast to other observers—rather extensive changes in the eye involving the ciliary body and lens; it is, therefore, possible that he used exceptionally high doses. Areas of necrosis in the liver and much infiltration with Kupfer cells is also reported by Kalt, whilst Koyanagi and Kinukawa (1937) report drop-like hyaline degenera- of the cells of the kidney tubules, though it should be pointed out that they used rather massive doses (30 c.c. septojod intravenously repeated after nine hours in one rabbit; 10 c.c. repeated three times after intervals of 2-3 days in another; and 5-10 c.c. repeated after an interval of one day or longer.)

Ophthalmoscopic and histological appearances—The ophthalmoscopic appearances seen experimentally and the histological findings as reported by the different observers—Riehm, Scheerer,

Umadzume, Sallmann, Vito, Homma and Kalt—constitute a clear-cut picture. Illustrations of the fundus appearances in rabbits are given by Riehm, Scheerer, Vito, Kalt and by Sorsby *et alia* (1937) and Sorsby (1940). (See also Figs. 1 and 2). The absence of pigmentary changes ophthalmoscopically in albino rabbits has been noted by Riehm and subsequent observers, but histological changes in the colourless pigment layer and the neuro-epithelium are stressed by Homma (1935).

The histological changes, as reported by different observers, constitute a clear picture. In the earliest stages the changes are confined to the pigment epithelium, which shows proliferation uniformly, with some heaping up here and there. At more advanced stages, active migration of the pigment cells, normal and altered, into the layers of the retina is seen, and the rods and cones become disorganized to the point of being unrecognisable as such. Some oedema of the ganglion cell layer may be present and occasionally some pigment cells may have migrated as far forwards, but essentially this layer remains unaffected. The choroid is not implicated at all. There is complete absence of any inflammatory or reparative reaction. There is some difference of opinion as to a subsidiary feature; Riehm described exudates between the retina and the pigment epithelium; these Scheerer regarded as artifacts; Homma more recently stressed massive albuminous exudate arising from the pigment epithelium and separating it from the retina, as an essential feature of the process.

Personal Observations

(1) *Dosage for experimental pigmentary degeneration of the retina.*—Previous observers, give the necessary dose for the rabbit as 5-10 c.c. of septojod intravenously. Ten c.c. are generally well tolerated, but degeneration can be obtained in most cases by one injection of 6 c.c. Within a week the ophthalmoscopic changes are unmistakable; within a fortnight they are fully established.

As for sodium iodate, it is not necessary to give repeated subcutaneous injections. One intravenous injection of 5 c.c. of the 2 per cent. solution gives satisfactory results (Fig. 3). The margin between the effective and lethal dose is narrow. For the fully grown rabbit, 2 kilos in weight, 4 c.c. may be ineffective, and 6 c.c. fatal. The solution of sodium iodate is best when freshly prepared. Old solutions undergo a change of colour, becoming yellowish.

(2 *Lesions in the viscera.*—A massive dose of sodium iodate, such as 8 c.c. of the 10 per cent. solution, is lethal within 20 minutes. Clinically air-hunger develops, the head is retracted and the animal dies during a fit of convulsions. Post-mortem extensive necrosis of the liver is present, histological detail being largely lost. With a dose effective for pigmentary degeneration

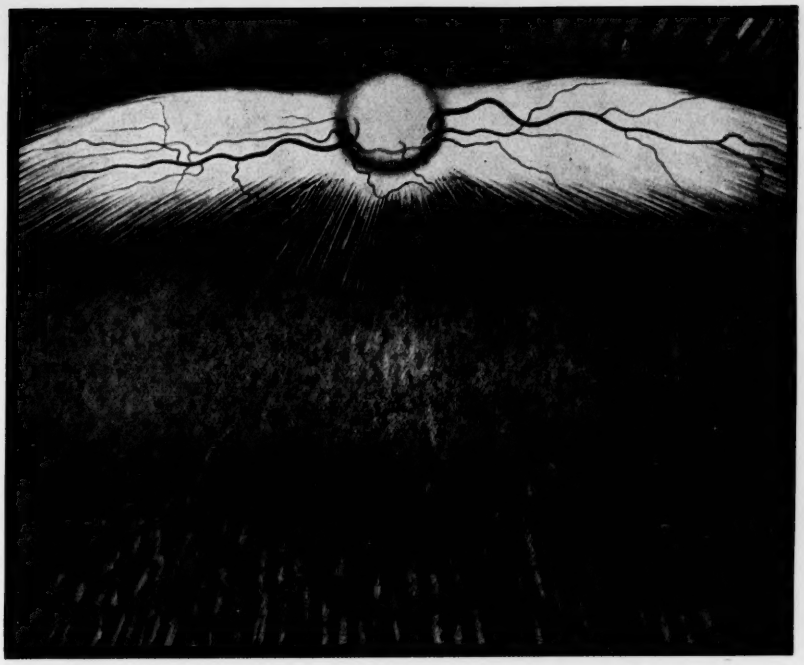

FIG. 1.

Rabbit's fundus showing pigmentary degeneration of the retina caused by intravenous injection of septogod.

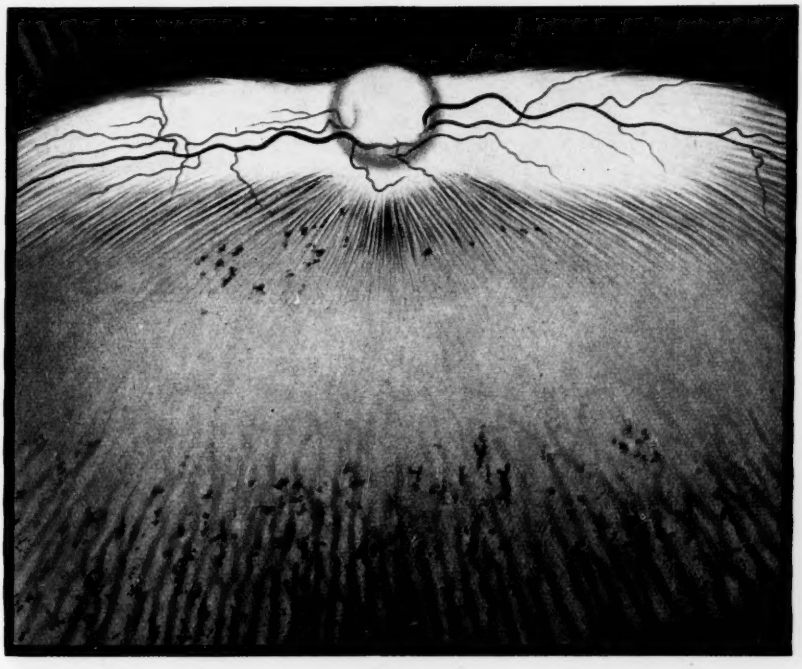

FIG. 2.

The same fundus as in Fig. 1 after intravenous injection of light green S.F.
From *Proceedings of the Royal Society of Medicine*, 1937.

of the retina, it is difficult to be convinced that the liver or kidney show any histological changes. This, however, does not exclude the possibility of functional damage of these organs. The changes reported by Umadzume, Kalt and by Koyanagi must be ascribed not to a dose effective for retinal degeneration but to toxic quantities.

In animals that have been treated with quantities of sodium iodate sufficient to induce retinal changes, and even in those that have two such effective doses (5 c.c. of the 2 per cent. solution), the liver on post-mortem examination failed to show any evidence of necrosis or of cellular infiltration. There was, however, well marked, cloudy swelling of the liver cells throughout the organ with loss of normal glycogen granules. No such changes were observed in control animals. These changes in the liver cells do not represent any permanent damage; indeed recovery was to be expected.

(3) *The changes in albino rabbits.*—The absence of ophthalmoscopically visible changes induced by septojod in albino rabbits, does not imply that the neuro-epithelium is not damaged. This was pointed out on histological evidence by Riehm and by Homma. Clinically this could be demonstrated by vital staining by the method described elsewhere (Sorsby, 1937, 1939, 1940.) The retina of the normal albino rabbit behaves like that of the pigmented animal in decolourising Kiton Fast Green injected intravenously. Albino rabbits treated with septojod or sodium iodate, whilst not showing any ophthalmoscopically visible changes, show staining of the fundi in the same way as treated pigmented animals—after a transient flush of colour in the fundus, no colour is seen, until the onset of gradually deepening coloration.

I am indebted to Dr. John O. Oliver for his kindly help with the study of histological preparations and for carrying out the experiments dealing with the effect of iodate on the liver. To Messrs. Butterworth & Co. (Publishers), Ltd., I am indebted for the loan of the colour blocks taken from Modern Trends in Ophthalmology, published by them.

Summary

1. A review is given of the clinical cases in which the use of septojod led to transient or permanent loss of vision from pigmentary changes in the retina.

2. The experimental work leading to the incrimination of sodium iodate as the toxic agent is indicated.

3. The dosage for the experimental production of pigmentary degeneration of the retina in the rabbit is shown as 5 c.c. of the 2 per cent. solution injected intravenously.

4. There is no evidence that with this dosage there is any permanent damage to other tissues, so that sodium iodate may be regarded as a selective poison to the retina.

5. By means of the method of vital staining with Kiton Fast Green it is shown that the retina is damaged by iodate in the albino rabbit though no pigmentary disturbances are seen ophthalmoscopically.

REFERENCES

v. BUNAU.—*Klin. Monatsbl. f. Augenheilk.*, Vol. LXXXIII, p. 345, 1929.
HOMMA.—*Arch. f. Ophthal.*, Vol. CXXXIV, p. 305, 1935.
KALT.—*Bull. Soc. Ophthal., Paris*, p. 304, 1937.
KOYANAGI and KINUKAWA.—*Arch. f. Ophthal.*, Vol. CXXXVII, p. 261, 1937.
OHM.—*Zeitschr. f. Augenheilk.*, Vol. LXXXIII, p. 339, 1934.
RIEHM.—*Klin. Monatsbl. f. Augenheilk.*, Vol. LXXVIII, p. 87, 1927; *Arch. f. Ophthal.*, Vol. C-CI, p. 872, 1929.
ROGGENKAMPER.—*Klin. Monatsbl. f. Augenheilk.*, Vol. LXXIX, p. 827, 1927.
SALLMANN.—*Zeitschr. f. Augenheilk.*, Vol. LXXX, p 342, 1933.
SCHEERER.—*Klin. Monatsbl. f. Augenheilk.*, Vol LXXVI, p. 524, 1926; *Ber. deut. ophthal. Gesellsch.*, Vol. XLVI, p. 315, 1926.
SCHIMMEL and RIEHM.—*Münch. Med. Wochenschr.*, p. 590, 1926.
SORSBY, ELKELES, GOODHART and MORRIS.—*Proc. Roy. Soc. Med.*, Vol. XXX, p. 1271, 1937.
SORSBY.—*Brit. Jl. Ophthal.*, Vol. XXIII, p. 20, 1939; *Trans. Ophthal. Soc. U.K.*, Vol. LIX, p. 727, 1939; Modern Trends in Ophthalmology, edited by F. Ridley and A. Sorsby, pp. 237-241, London, 1940.
UMADZUME.—Ref. *Centralbl. f. Ophthal.*, Vol. XXII, p. 836, 1929.
VITO.—*Boll. d'Ocul.*, Vol. XIV, p. 945, 1935.

THE NATURE OF EXPERIMENTAL DEGENERATION OF THE RETINA

BY

ARNOLD SORSBY

LONDON

In the preceding paper an account was given of pigmentary degeneration of the rabbit's retina induced by intravenous injection of 5 c.c. of 2 per cent. solution of sodium iodate. It was shown that the essential lesion was damage to the neuro-epithelium, the pigmentary changes being absent in albino rabbits, and that furthermore in doses effective for retinal damage, sodium iodate acted as a selective poison for the retina.

The selective action of sodium iodate on the retina, raised the question whether some specific retinal metabolic process was disturbed by this chemical. The possibility presented itself that the iodate—a powerful oxidising agent—destroyed or disturbed the

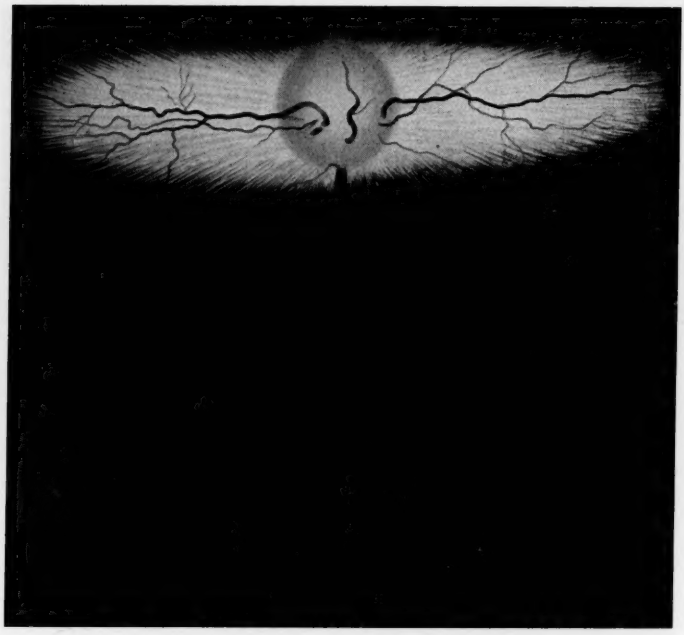

FIG. 3.

Rabbit's fundus showing fine pigmentary degeneration induced by intravenous injection of sodium iodate.

FIG 4.

Rabbit's fundus showing massive pigmentary degeneration caused by repeated subcutaneous injections of sodium perborate.

highly reducing vitamin C, present in exceptionally high concentration in the retina. *In vitro* the amount of iodate used experimentally destroys 266 mg. of ascorbic acid (vitamin C)—a considerable quantity in view of the small amounts normally present in the body. The high concentration of vitamin C in the retina is seen from its distribution in some tissues in man (Bessey and King, 1933), adrenals 2·0, liver 1·2, ovaries 1·5, heart 0·8, brain 1·8, mg. per cent., compared with the value of 18·9 mg. per cent. (Nakamura and Nakamura, 1936, for the retina and choroid in the rabbit).

Tahata, 1937, found that in a large series of mammals and amphibians the vitamin C content of the retina was high for all animals, being highest in toads (28·9 mg. per cent.), and lowest in dogs (10·7 mg. per cent.). The average content of the retina is about the same as for the lens, where the rôle of vitamin C in metabolism is well recognised. In view of these facts, an attempt was made to inhibit the development of pigmentary degeneration in the retina by the administration of vitamin C in doses of 0·25 gm. intravenously for three days prior to the injection of iodate. The results were completely negative. In animals thus treated pigmentary degeneration developed with the same regularity as it appeared in untreated animals. The action of sodium iodate cannot therefore be due to the destruction of vitamin C with a consequent actual or relative vitamin C deficiency in the retina, for the animals were saturated with the vitamin. The possibility of the iodate interfering with the consumption of available vitamin C remains. Fig. 1 shows the typical pigmentary degeneration observed in a rabbit treated with vitamin C prior to the administration of sodium iodate.

The possible rôle of vitamin C in retinitis pigmentosa is further suggested by the following note for which I am indebted to Dr. E. C. Dax.

"Controlled estimations of the urinary vitamin C output were made on five female and two male mental defectives with retinitis pigmentosa.

The output in the females was measured on three successive days, 300 milligrammes of ascorbic acid being given on the third morning. Both the cases with retinitis pigmentosa and the controls showed a vitamin deficiency. Accordingly 50 mgms. a day of ascorbic acid were given to each for a month and the estimations repeated. Four of five patients with retinitis pigmentosa and two out of the six controls still showed a gross vitamin deficiency.

The males were given 50 mgm. of ascorbic acid each day for a month before similar estimations were made. Both the experimental cases and the controls still showed a vitamin deficiency. After having 300 mgm. of ascorbic acid on the next three mornings, the controls excreted over 50 per cent. more vitamin C than did the cases with retinitis pigmentosa in the following 24 hours.

Thus six of seven patients with retinitis pigmentosa as against two of nine controls showed a vitamin C deficiency after supplementary feeding, although all had been having similar food for some years."

Sodium iodate is a relatively stable compound, but the question arises whether it is as stable in the bloodstream as *in vitro*. This involved testing for the stability of iodate in blood *in vitro*, in plasma, and in the bloodstream of the intact animal. Oxidising agents liberate free iodine from iodides in solution: the persistence of sodium iodate can therefore be shown by a blue colour when sodium iodide is mixed with a solution of starch to which a drop of dilute hydrochloric acid is added, and this mixture brought in contact with the fluid suspected of containing iodate. Both blood *in vitro* and plasma to which iodate in minute quantities (smaller than the amount that would be contained in a corresponding quantity of blood withdrawn from a rabbit previously treated with 5 c.c. of 2 per cent. solution of sodium iodate injected intravenously) did not destroy the iodate, for such blood and plasma still gave a distinct blue colour when added to a solution of sodium iodide and starch. It was otherwise with blood withdrawn from the rabbit after injection of sodium iodate. At least 20 drops of such blood withdrawn immediately after the injection of iodate were required before a doubtful blue colouration could be obtained in the test for iodine. The test repeated 10 minutes and 20 minutes later was completely negative. It would therefore appear that the iodate is immediately broken up in the bloodstream, and that its action on the retina is of an indirect character.

Another attempt at elucidating the nature of the action of sodium iodate was made by administering other oxidising agents to see whether a similar effect could be induced in the retina. The substances used were colloidal manganese dioxide, sodium perborate and potassium persulphate. The highest concentration of manganese dioxide that could be obtained in solution was 0·35 per cent.. and with this concentration massive doses would have to be injected to obtain a quantity equivalent to the effective dose of sodium iodate. Repeated injections of smaller doses (7 c.c., 10 c.c., 12 c.c., 15 c.c., intravenously on four successive days, the last dose being combined with 20 c c. injected intra-muscularly) gave a completely negative result. The use of sodium perborate and ammonium persulphate intravenously proved unfeasible, as 5 c.c. of the solution containing the equivalent amount of 2 per cent. sodium iodate (4·72 per cent. and 6·9 per cent. solutions respectively) were lethal, instantaneously in the case of perborate and within half-an-hour with persulphate. Persulphate also proved lethal when injected subcutaneously. Perborate was tolerated subcutaneously.; 20 c.c. of the saturated solution were injected on two occasions at an interval of a week. Ten days after

the first injection there was some lack of lustre in the area below the opaque nerve fibres; peripheral pigmentary changes were observed four days later, when a further subcutaneous injection of perborate of the same dose and concentration was given, to be followed by two more at weekly intervals. In all, five injections amounting to 100 c.c. were thus administered over a period of five weeks. Definite ophthalmoscopic changes were present, as already noted, by the end of the first fortnight: these gradually intensified and the appearances seen in Fig. 4 illustrate the condition after two months. These changes are different from those obtained with septojod or sodium iodate; instead of appearances simulating retinitis pigmentosa, the lesions bear some resemblances to an inflammatory reaction.

The suggestions that emerged from these findings were that iodate probably acts by virtue of its oxidising properties, and that the different appearances of the perborate lesion were probably due to the different rate of action, perborate in the doses and method used taking longer to induce visible changes.

What significance these findings have in the interpretation of the range of pigmentary changes seen clinically, is difficult to assess. That two different oxidising agents should produce changes simulating retinitis pigmentosa in one case and chorio-retinitis in the other, raises the question as to whether clinically observed pigmentary changes with their great ophthalmoscopic variations, are not fundamentally identical lesions, modified by a different rate of development. There is no inherent improbability in the suggestion that retinitis pigmentosa is caused by an inborn metabolic disorder and chorio-retinitis by comparable tissue-poisons introduced extraneously.

These results and observations are offered with considerable reserve. The work recorded presents the basis of a wider experimental study which is now indefinitely postponed. The results described have not been checked and they are published as a preliminary and unverified note.

My thanks are due to Mr. R. T. M. Haines, of Messrs. Crookes Collosol Ltd., for the supply of colloidal manganese dioxide, and to Mr. I. E. Weber, of Messrs. B. Laporte Ltd., Luton, for the supply of other chemicals used. To both I am obliged for their kind interest and guidance on chemical problems.

REFERENCES

BESSEY, A. O. and KING, C. G. (1933).—*Jl. Biol. Chem.*, Vol. CIII, p. 687.

NAKAMURA, B. and NAKAMURA, O. (1936).—*Arch. f. Ophthal.*, Vol. CXXXV, p. 87.

TAHATA, S. (1937).—*Acta Soc. Ophthal. Jap.*, Vol. XLI, p. 147.

CONVERGENCE

BY

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LONDON

CONVERGENCE may be summarised as consisting of three parts, tonic, accommodational, and fusional (Maddox). Tonic convergence is that amount of fusional innervation which is necessary to place the eyes in the position of parallelism at infinity.

The usual infinity distance in practice is six metres, at this distance actually 0·16 dioptres of accommodation and one prism dioptre of convergence are in use. Although Maddox suggested the term " Tonic " there is no reason for regarding this type of convergence as other than fusional, the same fusion innervation acts at distance as at the near point.

Accommodational convergence results from, and is associated with, any accommodational effort. These two functions are interconnected; contraction of the ciliary muscles is accompanied by a known and measurable amount of convergence. The contraction of the ciliaries may be insufficient or too great, but convergence must be exact for any point within infinity, to avoid diplopia. At the near point (33 cms.) eighteen prism dioptres are required, and as accommodation is variable, the final adjustment is known as fusional convergence.

If accommodational convergence is insufficient fusional convergence is positive (adductive), if it is excessive fusional convergence is negative (abductive).

All lateral muscle imbalances are errors of convergence, and all tests are convergence tests. Fusional convergence is the innervation, which corrects near point imbalances. In order to judge whether or not any imbalance, either at distance or near, requires help to maintain efficiency, the exact *fusional reserve* which the patient possesses must be known.

The fusional amplitude can be ascertained by taking the patient's duction, which roughly represents the fusional amplitude, which may enable him to cope with the imbalance.

Any imbalance at the near point is always the difference between that measured at distance and that found at the near point (33 cms.). For example if three dioptres of exophoria is found at distance and five dioptres at near, the sum total of the near imbalance is two dioptres of exophoria, whereas if three dioptres of esophoria exists at distance and five dioptres of exophoria at near, the sum total will be eight dioptres of exophoria at the near point.

Physiological Exophoria

A certain amount of exophoria at the reading distance, provided that it does not exceed six prism dioptres (P.D. 60 mm.) is normal, and must be looked upon as a *normal convergence lag* due to the fact that accommodation is not exerted to the value of the fixation distance. In viewing ordinary print at 33 cms., we converge exactly eighteen prism dioptres; but three dioptres of accommodation are not in use, the amount is 2·05 D., or less, because average reading matter subtends a visual angle of not more than 6/12. Snellen.

This normal convergence lag is supplied by fusional convergence and indicates a normal shortage of accommodational effort.

Physiological exophoria permits a certain amount of hypermetropia to be tolerated without upsetting the muscle balance.

Diagnosis of Convergent Imbalances

In testing convergence imbalance we measure the tendency, relative convergence or divergence, of the visual axes at any point of fixation; and this should be done before and after the refractive error has been corrected, as often an accommodational convergence error is neutralised by correct lenses.

The imbalance in prism dioptres having been found, we ascertain if the opposing duction is able to cope with the error.

The following are four very useful tests which can be made to investigate the presence of insufficient or excessive convergence.

The Cover Test

This is perhaps the most accurate method for examination of any convergence imbalance. It is equally accurate for both distance and at near.

The ordinary dissociation tests, such as Maddox rod or wing test, or the procuring of diplopia by means of vertical prisms, though they prevent fusion, do not remove the desire to fuse, there is a tendency to align the diplopic images. The cover test not only prevents fusion, but removes the desire to fuse.

Snellen 6/9 line is used as a fixation target for distance, and the point of a pencil, for near.

In cases of established presbyopia the reading correction must be worn for testing at 33 cms. in addition to that necessary for distance.

The eyes fix the target, and an ebonite disc is placed over one eye, on removal an IN (exophoria) or an OUT (esophoria) movement of this eye is seen if any imbalance is present.

The imbalance can be accurately measured with base-in prisms

(exophoria) and base-out prisms (esophoria), the strength of the prism which prevents movement being the measure of the imbalance. The actual position of the eye under cover can be seen, if a green (red free) light is used as a target. A polarised glass screen (the analyser) is placed in front of the light and a second screen (the catalyser) in front of the eye under examination, at right angles to the analyser.

The polarised screens prevent the patient from seeing the light, while the examiner can clearly see the position of the eye under the screen.

The Prism Stereoscope Test

This is a very reliable test for estimating convergence stability at the reading distance. Javal's F.L. card is placed at 33 cms. upon the bar of the stereoscope with the septum in such a position that F. is seen with the left eye, and L. with the right eye.

Nine prism dioptres are placed before each eye, with bases OUT, representing the normal amount of convergence in use for this distance, presuming that the P.D. is 60 mm.

If convergence is normal the observer using both eyes sees E. In cases of insufficient convergence L. is seen with the left eye and F. with the right eye, if over-convergence is present F. is seen with the left eye and L. with the right eye.

The prisms must be reduced in the case of insufficiency and increased in the case of over-convergence to obtain fusion.

The amount of exophoria or esophoria will be the difference between eighteen prism dioptres and the total amount of prism power which is required to form E.

Small letters, which are seen as Y.Z. upon the vertical limb of the E. indicate a high grade binocular stability, in which the macula lutea is in use. If Y.Z. is seen, any degree of hyperphoria can be ruled out.

Convergence efficiency, must be determined by prism-convergence at 33 cms., the ordinary reading distance.

A test made with a small object or light as the fixation point, which is made to approach the end of the patient's nose, while the exact distance at which diplopia is noted, or the observer records

deviation of one eye or displacement of the central light reflex of this eye, is loaded with inaccuracies.

Factors arise which do not occur at 33 cms.

Excessive accommodation on the approach of the object stimulates convergence, and the images on the retinae become enlarged, owing to shortening of the distance between the object and the nodal points of the eyes examined.

Convergence may also be stimulated by the fact that the patient is aware of the increasing nearness of the fixation point. In early presbyopia, which results in the receding of the near point, the object becomes blurred, this tends to inhibit fusion and to cause diplopia. For these reasons convergence efficiency or insufficiency cannot be diagnosed by this means.

These near imbalance tests measure the amount of fusional convergence in use.

A maximum of six prism dioptres of exophoria is a convergence lag representing a normal shortage of accommodation.

A greater amount of exophoria than normal is suggestive of insufficient convergence, while less suggests an increased accommodative effort due most probably to hypermetropia.

In *early* cases of presbyopia a lag of less than six-prism dioptres of exophoria is frequently found, because the hardening lens requires a greater ciliary effort to alter the curvature for near vision; the proper reading addition restores the normal physiological exophoria.

Ductions

Duction is the measure of the amplitude of fusion reserve. Duction describes the innervation which will cause the eye muscles to move in the interest of binocular vision.

First grade fusion must exist before duction can be estimated. We measure the power the eyes have of maintaining binocular vision against the diplopia producing effect of prisms.

Adduction is the amount of convergence which can be exerted irrespective of accommodational convergence.

The measurement, both for distance and near is made with base-out prisms before the eyes, geared together so that equal amounts can be rotated simultaneously. The power is increased until the image blurs, which means that accommodational convergence is called into use. This blur point measures the fusional convergence amplitude.

If prism power is added until diplopia is produced the limit of accommodational convergence has been reached.

The prisms are now reversed until the prism power recording fusion is ascertained. The recovery point is of some importance as

insufficient convergence usually has a very low recovery point. Normally the recovery point is half the amount of prism power which produced diplopia.

Normal adduction at distance measures eighteen prism dioptres to the blur point, and twenty-four prism dioptres before diplopia occurs.

At the near point thirty prism dioptres can be overcome.

Abduction is measured with base-in prisms and since divergence cannot stimulate accommodation, the prism power causing diplopia is the measure of abduction.

Normal abduction at distance measures eight prism dioptres and at the near point eighteen prism dioptres is the measurement.

Supra and infra-ductions are measured in the same way with vertical prisms. The amplitude of supraduction measures two prism dioptres and infraduction three dioptres.

A slight degree of hyperphoria when corrected often makes the treatment of esophoria much easier. If duction reserves are normal many imbalances cause no symptoms whatever.

Treatment

The treatment of heterophoria is very briefly outlined as follows :—

Exophoria with a low adductive reserve, may be refractive or pathological. Hypermetropes with exophoria should not as a general rule be given plus lenses which increase the near point imbalance, reduced lenses will often reduce the exophoria which shows that it was of the exhaustive type.

Insufficient convergence, where the general health is not the cause of the high exophoria, responds readily to orthoptic training. Exercises with increasingly strong base-out prisms, on either the variable prism stereoscope or the synoptiscope will increase adduction amplitude, in a few weeks, and provide a reserve whereby exophoria at the near point can be overcome.

The stereoscopic sense, which is always of a low grade type, is greatly improved, and suspension of vision in one or the other eye will no longer take place.

In well established presbyopia showing a high exophoria at the near point, base-in prisms incorporated with the reading addition, will prove satisfactory.

Esophoria with a low adduction is much more uncertain in its treatment.

As, however, it is often due to hypermetropia either latent or manifest, refractive correction is all that may be needed.

When the correction eliminates the distant imbalance but has no effect on the near, a bifocal addition irrespective of age, will give comfort when reading.

In other cases, when general pathological causes can be ruled out, orthoptic training with base-in prisms may be tried, with the hope of increasing the abduction reserve.

The wearing of permanent weak base-in prisms (which must not cause diplopia) can be prescribed at the same time.

As a temporary measure, in older patients, who have to do much close work relieving prisms (base-out) must be ordered.

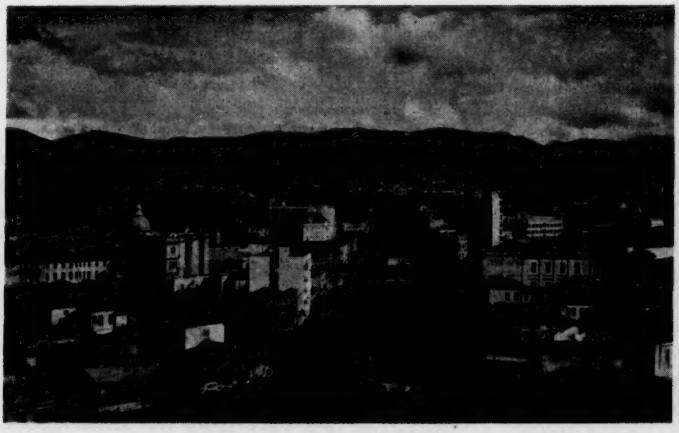
THE THIRD BRAZILIAN CONGRESS IN OPHTHALMOLOGY. JULY, 1939

BY

E. E. CASS

LONDON

ON Wednesday, July 5th, in company with Professor Linneu Silva, Professor Moacyr Alvaro, Professor Correo Meyer and Dr. Assis Brasil, I flew from Rio de Janeiro to Bello Horizonte, the capital of Estado do Minas Gerais, where the Third Congress of Ophthalmology was being held. We had to fly high, as the country is very mountainous and our descent was too sudden to be pleasant. We were met by Professor Santa Cecilia, the President of the Society and by Dr. Hilton Rocha, the Secretary. We were awaited with some curiosity, as Professor Silva had sent a telegram



Av. Aff. Penna—Bello Horizonte.

in Rio, in which he had written: "Arriving by plane, Moacyr, Miss Cass and self," but unfortunately, the English name was too much for the Brazilian clerk and the telegram read: "Arriving by plane, Moacyr, Moses and self."

Although winter, the sun was warm and the air clear and exhilarating. Bello Horizonte is a beautiful little town with broad streets and flower-beds and is situated on high ground and was planned and built in 1886 as the capital of the state. Alvaro remarked that if my English friends knew I was 300 miles north of Rio, they would think that I was living amongst Indians. The little hotel was clean and comfortable and its excellent laundry and pressing service would set a good example to many of our hotels.

As the Congress officially opened later in the day, Moacyr took me to the very modern museum, where one saw the beautiful stones of Brazil, precious and semi-precious in large quantities. Brazil is also rich in the most beautiful woods and the residential quarters of the cities have most attractive houses, the Brazilians seeming to have a great ability for building attractive and original residences. The museum also showed us the flora and fauna and industrial products of various parts of Brazil. Twenty years ago, they manufactured very little and quite a lot of their boots and clothes were obtained from England, and they are very proud of their progress in manufacturing their own materials. The custodian thought we were both English and said in Portuguese to his friend: "They have come to steal our wealth."

My first lunch at Bello Horizonte was astounding on account of its size. Its cooking was excellent. Unfortunately, I thought the first course of assorted cold meats was the main one and ate heartily of it, only to discover to my dismay that it was followed by soup, fish and a Brazilian entree made of spaghetti and spiced meat and after this, two meat courses and then jellies made of bananas and quinces which are eaten together with milk cheese. It was here that I first met Professor Penido Burnier and his family, and for this man I have an intense admiration. He lives in the provincial town of Campinas, where, twenty years ago, he started his own Institute of Ophthalmology in a small house with beds for twenty patients. I was lucky enough to be invited to lecture at his Institute, which has now grown from that one small house into a flourishing clinic. Ophthalmology, as practised in Brazil and the Argentine, is very different from our arrangements here, and I think we may learn something from them in this respect. The hospitals are simply for the poorest of the poor who can pay nothing, and ophthalmologists run their own clinics and the patient who has anything wrong with his eyes goes straight to one of these clinics. Usually, the fees vary from ten shillings to £1 and therefore almost anyone can get the best advice for a moderate

fee. This relieves the hospital clinics and caters for the large body of people, who, in this country, have to come to our hospital clinics as they cannot afford a specialist's fee, but incidentally can afford to pay something and would rather do so if it could be arranged. At the Institute of Penido Burnier, there are now eight ophthalmologists working and five ear, nose and throat surgeons. Each ophthalmologist has his own consulting-room, and everywhere there are modern instruments. Besides these clinics, there are modern and well equipped X-ray departments and laboratories. There is a room for lectures, meetings, etc., provided with an epidiascope and film projector. The Ear, Throat and Nose Clinic is the most modern and has beautiful furniture and a comfortable waiting-room with flowers and magazines. There are three classes of in-patients: in the most expensive, each patient has his private bedroom, sitting-room and his own bathroom; in the second class, there are private bedrooms but no sitting-rooms and they share bathrooms: the third class is for the very poor, and it consists of little wooden bungalows. On the veranda of one of these, I saw an old negress who had been a slave in the 'eighties waiting for an operation for cataract. In the clinic itself, I was lucky enough to see two cases of cysticercus causing detachment of the retina. One cannot help admiring the man who had the ability to found such a clinic and make a success of it, especially when one considers the difficulties of transport in an enormous country like Brazil.

My first day at the Congress was handicapped by the fact that I spoke Spanish and not Portuguese. Although there is a great similarity of the language, the accent of the Portuguese as spoken in Brazil is very difficult to follow.

The Inaugural Session of the Congress was held that evening in the Automobile Club. About eighty ophthalmologists were present, also some of their families attended. Moacyr had previously told me that they realised that some bad papers were produced, but he said that it was necessary to encourage people to come. Brazil is an enormous country and many had travelled from two to five days to get to the Congress and I met one man who had travelled as many as eight days. Moacyr said that if a man felt he could read a paper it would encourage him to come, and if he came, he would have an opportunity of learning something. If he was any good, he would realise later that his paper was a bad paper, but would be encouraged to work and produce something better. It is very essential that the Brazilian ophthalmologists should come to their congress for some of them are shut away miles from any centre of ophthalmology and it gives others a chance to discuss ophthalmology with other ophthalmologists and to learn new methods.

Thursday, July 6.—On Thursday morning, I left Moacyr busily

typing his paper. He is one of the most energetic people that I know. He works until nine o'clock at night even on Saturday and produces papers and translations etc., as well. He speaks English like an Englishman and German like a German, also French and Spanish. He is always late because he has too much to do. I once asked him to dinner in London and two hours after he was invited, he walked in quite calmly, although the cook was almost having hysterics.

An ophthalmologist of Syrian extraction took me to swim at the Tennis Club. It was a very beautiful, large, modern, clean bath, but to our amazement we found that no-one was allowed to swim without a medical certificate. When we did find this out, Dr. Ferriche had already donned his trunks! We were accordingly accompanied by the Secretary to the Doctor, who lived about five minutes away, Dr. Ferriche being attired in dressing-gown and no shoes! The Doctor obligingly gave us certificates without examining us and also delayed us by showing us his statistics. No people with tuberculosis, uncompensated heart disease, skin disease, obvious manifestations of venereal disease, etc., were allowed in the bath. He had statistics on how graded swimming exercises improved the health in various diseases. There was also a small bath for children and he had statistics on the improvement in health of all the school-children of Belo Horizonte due to exercises, etc. He was a most hard-working, industrious young man and would have talked all the morning if we had let him. By the time we got to the bath, the sun had nearly disappeared and that water was the coldest thing I had met for a long time.

At two o'clock, the real work of the Congress began, the first paper being an excellent work by Correo Meyer on the " Ocular manifestations of disturbances of metabolism." He spoke a good deal on the metabolism of lipoids and included in his work observations on cases of Tay-Sachs, choroiditis, Niemann-Pick, Spiel-Meyer degeneration, etc.

Penido Burnier then gave a well-illustrated and interesting paper upon " ocular cysticercus." He said that since 1924, 102 cases of ocular cysticercus had been found in Brazil, 74 of these being in his own clinic and in one of these cases both eyes were affected. Cysticercus could appear in the conjunctiva, the vitreous, the anterior chamber and in front of, or behind the retina. It was always as well to suspect this disease in detachment of obscure origin. In cases of cysticercus of the conjunctiva, the scolex could be seen in the cyst. Cases affecting the retina showed detachments and cataract complicata—and it was sometimes difficult to diagnose from a retinal cyst. The complement fixation test was a positive proof, but on the whole, when the disease affected the interior of the eye, it was not easy to diagnose. He had seen it in one eye that

had been removed because a diagnosis of sarcoma had been made. Dr. Silva then quoted another case in which a cataract had been removed and then a cysticercus was found in the vitreous. Dr. Belfort Mattos of Sao Paulo showed some retinal photographs. Dr. Conti gave a short paper on his experiments upon retinal circulation and the session ended.

All through the sessions of the Congress they used to produce small cups of strong black coffee and, believe me, it was necessary when some sessions of the last days went on into the small hours of the morning. Brazilians are without the inhibitions of the English and all meetings lasted for a long time as most papers were freely discussed.

Malbran, who is a charming and hard-working Argentine ophthalmologist, arrived that evening. He and Adrogue have written an excellent book on " Squint."

Friday, July 7.—The whole of Friday's sessions was given up to the consideration of the problems of trachoma. Work started at 8 a.m. Dr. Lech, who works in Penido Burnier's clinic, spoke of his experiences of the treatment of trachoma with sulphanilamide. He had a group of cases treated with and without this drug and his conclusions were that on the whole this drug was of some use in the treatment of this disease. A lively discussion followed, where the general consensus of opinion seemed to be that up till now its utility had not been established. Various other papers were then read upon trachoma in Brazil and its treatment.

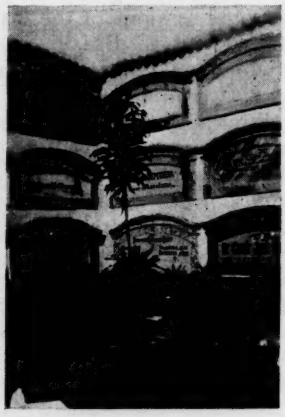
In the afternoon, the whole Congress departed in cars to visit the iron mine " Siderurgica Belgo-Minera." It was a most exciting ride. We wound round and round the mountainside on earth roads which periodically get washed away and are full of stones and potholes and our Jehu had ideas about driving. At first, it was a terrifying experience and after a nasty skid at one corner, Moacyr expostulated on his speed. The drivers on our expeditions were usually negroes and mulattoes and always joined in our conversations. I liked the negroes of Brazil; they are quite different in character from the North-American negroes and there is not the same colour bar in this country and the negro has none of the inferiority complex of the negro of North-America; they are, in consequence, very pleasant people.

The hills were dark green in colour, so unlike our English green, with reddish patches of earth and rock and few trees and the dust was appalling.

First, we visited the charming old Indian village of Sabara. Here was the typical Brazilian plaster and wood church, very ornate and grand inside, with brightly coloured images in rather tawdry vestments. Opposite was the cemetery with the coffins in the wall. Here I took a photo and funnily enough, when I printed it, the tomb I had focused was that of a doctor.

At the iron mine, we got covered with still more red dust and after having seen the furnaces and how the molten iron ran into troughs and how the red-hot iron blocks were flattened into long thin bars, we retired and had tea, consisting of beer or lemonade and sandwiches at the club belonging to the mine.

Norsa Senhora do Carmo-Sabará.



Cemiterio, im Sabará.

Group of Congress at the iron mine.

After dinner, I was too weary to attend the evening session, as the strain of following the Portuguese and the change of altitude after staying at Rio was too much for me. In fact, the Brazilians wore me out as they started their days at 8 a.m. and ended in the small hours.

Saturday, July 8—The next morning, I overslept and found that the Congress had departed to two different hospitals to see operations. I chartered a taxi and requested to go to one hospital. On arrival, the porter seemed rather surprised at my request to be taken to the operating theatre and was even more puzzled when I said that all the Congress was there. Finally, I was shewn into a waiting-room and when a lady in an advanced stage of pregnancy was shewn in, my suspicions that I had come to the wrong part of the building were confirmed! Finally, I was rescued by a kind gynaecologist and driven round in his car to the ophthalmological block.

I saw a modified Toti's operation very nicely and neatly performed, the operator using his own particular forceps, which were also a needle holder and seemed very handy for sewing the mucous membrane of the sac to the mucous membrane of the nose. After this I was requested to examine a doctor's child with a squint, which was the result of a birth injury, due to contracted pelvis and forceps delivery, and combined with muscular paralyses, the right eye was blind. I was very sorry for the mother and father as the mother had nearly died on delivery and was told not to risk another child.

At 2 p.m., Malbran read an excellent paper on the pathology of strabismus. He stressed the fact that the cause of squint is not one, but many. He discussed the general factors and the ocular factors and showed how it is impossible to group all squints under a common denominator. He realised also how difficult it was to get a perfect classification for all cases of strabismus. Among his final conclusions, he said that anatomical factors must first lead to anomalous positions of the eyes, combined or not with factors of innervation and that he could not agree that weak fusion was a principal cause in determining a squint. This paper, read in Spanish, was much appreciated and applauded. After this, the Doctors Campos of Rio read a paper on submucous resection of pterygium. Dr. Robin of Rio read a paper on cyclodialysis in choroido-retinitis and uveitis with hypertension and Dr. Borges Dias of Rio a paper upon heterophoria due to visual fatigue.

After this session, I had my first meeting with Arruga, who had come to Brazil to operate upon President Vargas's father. We were entertained at a cocktail party at the museum and had a quiet evening afterwards as there were no further lectures that evening. He was extraordinarily kind to me, as he read and corrected all

my six lectures on squint, written in my bad Spanish and it was Arruga who made the epidiascope work for me and projected my film for me in Rio. He is simple, unassuming and friendly with all and is much beloved by the Brazilians.

Sunday, July 9.—Sunday was given up to social amenities. In the morning, we went to the tennis club where people amused themselves in divers ways, most of them sitting on the roof drinking cocktails and watching the swimming and sports. We had a most hilarious lunch, we being Moacyr, Malbran, Arruga and an Ear, Throat and Nose specialist named Leité. Arruga is no mean raconteur and he gave us amusing tales of Gonin's absentmindedness. Apparently, Gonin never could keep an umbrella and so finally his wife would only buy him cheap ones; this annoyed Gonin so much that he went and bought himself a beautiful expensive umbrella! He arrived home triumphant and said to his wife: "Look at my beautiful new umbrella!" "Where?" she demanded. Gonin looked down; in his hand was an old decrepit monstrosity of an umbrella. On his way home, he had been to see a patient and had left his beautiful umbrella at the patient's house! We laughed so much that various other oculists joined us and finally Arruga broke up the party with a very witty but rather broad story and then said: "This is dreadful; when Miss Cass returns to England and they ask her what kind of a man is Arruga, she will say he is a man who tells dreadful stories!"

That afternoon, we were all commanded to the Governor's palace. He lives in a beautiful house, facing a long row of tall trees. From his windows are views of the hills and his own garden and flowers. We all shook hands with him, various speeches were made and then we shook hands again and departed.

A garden party at the waterworks, given by the Minister of Health, was the next item on our programme and all Bello Horizonte turned out in its best to greet us. We had tea on a terrace and, as the sun fell the orchestra started to play and dancing began. Brazilian dancing is very energetic and consists chiefly of "Machichis" and "Sambras," which are negro in origin.

I was too weary after this to visit a native fair, where Alvaro told me that unfortunately I had missed some excellent negro dances.

Monday, July 10.—Our last days at Bello Horizonte were interesting but crowded and we were all tired. Monday we left the hotel at seven a.m. to visit the gold mine of Morro Velho. Once more we had this perilous journey over the mountain road, branching off on another track before reaching Sabará. This gold mine is owned by an English company and there is a colony of 300 English people, consisting of the officials of the mine and their families. Funnily enough, when I reached home one of my first patients was an English girl, born in Morro Velho, whose family

still live there. The entrance to the grounds of the company are beautiful with palm trees, tropical shrubs and cultivated gardens. We were met at the guest house by an Englishman, who looked as though he wondered what in the world an English woman was doing mixed in with a crowd of Brazilians! It was really rather amusing and Moacyr and I had a quiet laugh over it. We were not allowed down the mine, as there were nearly a hundred of us and anyway, the miners consider it bad luck for women or priests to descend the mine. The ore in this mine is treated to a series of crushings and washings to remove the gold and also to treatment by chemicals to remove impurities. Finally, we arrived at the melting house and saw a solid bar of gold weighing 60 lbs. and worth £4,000. There was a general rush, amid much laughter to catch hold of all this wealth. During our wandering through the grounds of the mine, I snapped Arruga in company with our official photographer who went everywhere with us. This gentleman was so pleased at the honour of being photographed with Arruga that, on condition I gave him the negative, he developed all my films free of charge. In South America, the first people who greet you are the press photographers and press agents and much to my indignation they woke me at 8 o'clock my first morning at Rio and asked if they could come up to my room and photograph me. I declined vehemently, but they waited patiently for an hour until I arrived downstairs. Our official photographer was very nice, whilst the press agent at Diario was a simply beautiful curly-headed Adonis, who said, "Oh, Miss Cass, you give me an interview and let us be photographed together." Somehow I gave him the slip.

The Committee and President were chosen for each session of the Congress. That afternoon, as the subject was that of "squint," they paid me the honour of asking me to be on the committee. Professor Linneu Silva of Rio read an excellent paper on the medical treatment of squint, which he said was the foundation of the treatment. There were various and many factors in the aetiology as Malbran had already stressed and a squint must be regarded as a symptom. He said that orthoptic treatment was indispensable for restoration of function as a complement to the aesthetic treatment, which was that of operation. Moacyr Alvaro then followed with another extraordinarily thoughful and well written paper on the surgical treatment of squints. He gave an extensive historical survey of the subject accompanied by lantern slides and diagrams and showed from statistics taken from many authorities that tenotomy was a bad operation. These two papers and the discussions that followed took up most of the afternoon.

At 9 o'clock, the session started again. Professor Pimentel spoke upon Marcus Gunn's syndrome. He had observed that his

" jaw-winking " is of common occurrence in cats when they are eating, the phenomenon occuring on the side of the face the cat is using for mastication. He illustrated this by an amusing film, in which he showed a patient with this conditon and then some cats eating. He suggested that Gunn's syndrome was really some atavistic phenomenon which some people showed also in being able to waggle their ears, etc. Two ophthalmologists then obliged, one by waggling his ears and the other his scalp, but the doctor who stole the show was a man who could do both at once! After much laughter, the business of the evening was resumed. Professor Pimentel kindly lent me his film to show at the Royal Society of Medicine, which I did in the Spring of last year.

Professor Leité then read a paper on tumours of the conjunctiva. Dr. Barros's paper on the appearance of leprosy in the anterior segment of the eye was read by Moacyr Alvaro. It was an excellent paper, beautifully illustrated by the author's own paintings. When I later went to Sao Paulo, Dr. Barros took me to the leper colony of Padré Bento where I saw case after case of nodules on the conjunctiva, corneal nerves with nodules of leprosy, cauliflower growths on the iris, small multiple nodules on the iris and keratitis, etc. He had made an exhaustive study of leprosy on the eye and had some wonderful material of what is rather a disheartening condition to deal with.

The following papers were also read :—

DR. SANTA CECILIA on " Persistent pupillary membrane adherent to the cornea."
GERALDO QUEIROGA (Bello Horizonte) on " Consideration of the blue appearance of the fundus of the eye following the use of methylene blue."
CONDE (Bello Horizonte) on " Atrophy of the papilla following the operation of Caldwell Luc."
DR. ROCHA and PAULO ELEJADA (Bello Horizonte).—" Concerning the classifications of glioma of the retina."
DR. MACHADO on " Neuro-epithelioma of the retina."

The discussion continued until 2 a.m., but I am afraid that at midnight I faded out.

Tuesday, July 11.—We were invited by the Governor to view the model Agricultural College and Farm of Florestal. We proceeded by cars over the usual dusty, but this time not so perilous, road and after a journey of about 2½ hours, arrived at a most beautiful spot. Surrounded on one side by hills and shrubs and on the others by miles of undulating plains lay the College and farm buildings. We drove to the Manager's house which was squarely built and surrounded on three sides by a veranda. We had been invited to a " Churrasco." Behind the house, tables were laid and an orchestra was playing and at the far end of the tables the meat was cooking. " Churrasco " is the most delicious meat in the world. Whole sides of young pigs, lambs, etc., are soaked over-night in herbs and spices and then next day a trench

is dug in which is placed a wood-fire. When there are nicely glowing embers, the meat, with spikes driven through it into the ground, is placed round the fire and cooked. The Governor also supplied marvellous wines and the waiters brought round the whole joint on its spike and carved off any piece for you that you fancied. After lunch, speeches were made, when, to my horror, they yelled my name and I was pulled to my feet by the doctors next to me. I then made my maiden speech in Spanish. All I could think of to say was how pleased I was to be in South America after wanting to come for such a long time, how beautiful their country was, and how, although I was a complete stranger and the life in their country was so different from my own, they had been so kind to me that I felt completely at home. I then sat down rather abruptly, but they seemed quite pleased and were very polite about it, as always, and all was well. After lunch, we visited the cows which were in the cleanest stalls I have ever seen. Someone heard I wanted to see the horses, so a groom was fetched and the Governor, a few others and myself went to the stables where a beautiful black horse was produced. The groom said I might ride it, but I was dressed in a cotton frock so I had to refuse with much regret on *my* part (I do not know about the horse!). The party ended at the guest house of the College, where we danced in the patio, more sambras and machichis, finally joining hands and dancing in a ring in and out of the patio. With much regret, we had to return to Bello Horizonte after a perfect day, so as to attend to the business of the Congress once more.

Once more at 8 p.m., we started with the following papers (and once more the session ended at 2 a.m.):—

CORREO MEYER (Porto Alegre).—"Contribution to angioid streaks of the retina."
PAUL PIMENTAL (Niteroi).—"Consanguinity and hereditary disease."
ALMEIDA and BURNIER JUNIOR (Campinas).—"Adiposis of the Cornea."
PAIVA CONCALRES (Rio).—"Results obtained in some cases of atrophy of the optic nerve by combined medical and surgical treatment."
GERALDO QUEIROGA (Bello Horizonte).—"Considerations on the change in acidity of the vitreous in glaucoma."
HILTON ROCHA (Bello Horizonte).—"Geron-toxon duplex."
JONAS ARRUDA (Rio).—"Cutaneous and ocular avitaminosis A."
MOURA BRASIL (Rio).—"Surgical treatment of retinal detachment."
CYRO DE REZENDE (Sao Paulo).—"The cornea of the corpse as material for corneal grafting."

Wednesday, July 12.—Arruga operated at one hospital in the morning, but, unfortunately, I never saw him as I had to wait for Moacyr and had to see a child with a squint at another hospital. Luckily, I had Moacyr's little instrument for measuring the angle, but otherwise I had nothing. It was a child of eleven, who had not even worn its glasses and I was quite sure that it had a false correspondence. I had been left with two cheerful young assistants to supply all my needs, but, alas, there was only an antique stereoscope! However, I had a brain-wave; with the aid of a mirror

from my bag, a torch and the perimeter and my knowledge of the angle, I solved my problem. It was a Heath Robinson apparatus, but it gave me ideas for further use. The child had a false correspondence! But I still regretted not seeing Arruga operate!

We then had a farewell lunch in the hotel, during which lunch, various people had to leave and catch trains and it was a hilarious affair.

At 2 p.m., the last session started. This session was followed by discussing arrangements for the 4th Congress and the meeting

Arruga operating.

broke up at 8 p.m., with the final closing session commencing at 9 p.m.

The papers read were :—

DR. ALMEIDA (Campinas) (Read by PENIDO BURNIER).—"Ten years of the surgery of cataract."

DR. SEMERARO (Barbacena).—" Intra-capsular extraction."

DR. TAVARES.—" The treatment of symblepharon by a contact glass."

DR. DONATE VALLI (Varginha).—" Our experience in 57 dacryo-cystotomies according to the technique of Dupuy-Dutemps."

DR. AURELIANO FONSECA (Sao Paulo).—" Associated movements of the maxilla and upper lid—(acquired form)."

DR. CARLOS ALBERTO CORREA (Bello Horizonte).—" Traumatic ophthalmoplegia sensory—motor."

The closing session was attended by the Governor and after some speeches, the Congress terminated with a most enjoyable ball and again more energetic Brazilian dances.

There is one little thing I would like to point out; that is, the

custom for speakers both in Brazil and the Argentine to read their papers sitting down and I think the idea is an excellent one. One can speak better when one is comfortable and it gives the nervous person confidence.

The following morning, we had rather a rush to get to the airport in Moura Brasil's car. There I took an amusing photo as a momento. Arruga, Moacyr and I then returned to Rio, all rather

Group of some of the members of the Congress with Malbran at right centre, front row.

weary and Moacyr and I had lunch at Alba Mar, both horribly deaf and neither being able to hear a word the other said. After that, Moacyr returned to Sao Paulo and I had a few days' rest before starting my lectures in Rio.

I was exceedingly glad to have been able to go to this Congress in a country so far from my own, but was only sorry that my knowledge of Portuguese hindered my understanding and appreciating more of their scientific work. I can never forget their extreme kindness and hospitality to me and only hope that one day I may be able to repay it in a similar fashion. I would like to pay a tribute to the organising ability of the Committee at Bello Horizonte, whose management of a hundred or more people was so excellent and whose arrangements never suffered a hitch. I would also like to thank that magnetic personality, Moacyr Alvaro, for all his consideration and kindness to me, for his extreme efficiency in organising my visit to his country and for being the chief instigator of my " rolling down to Rio."

ANNOTATION

Interaction of sense organs

In the past musicians have believed that there is a close connexion between colour and tonality. In the score of the "Prometheus" symphony, Scriabine indicated the colour and light effects that should accompany the performance of this work. His idea was carried out on two occasions, once in Moscow and at another time in the United States. The finale of the symphony, which the composer conceived as a mighty crash of sound, he wanted accompanied by dazzling light. In this experiment the author was guided entirely by his own subjective emotion, and science, in the Soviet Union, is making valuable contributions to the study of the interaction of the sense organs. Wedensky, some years ago established the fact that music sounds louder to the auditor when the concert hall is flooded with light, and that the volume of sound lessens when the light is dimmed.

Soviet experimentalists have established that not only do visual irritants affect hearing, and auditory irritants, vision, but that the stimulation of any sensory organ, whether external or internal, may affect all other sense organs. Thus, visual irritants may heighten the sense of taste, sound irritants, temperature, taste and smell change, perception of colour.

Professor Kravkov, of Moscow, has found that the ability to perceive colour changes varies to a considerable degree if one warms one's hands or smells some odour, *e.g.*, bergamot oil, or if one holds a lump of sugar in the mouth. It was found that in all these cases red, orange and yellow appear dimmer and are less visible, whereas green, blue and violet are intensified.

These facts, taken from an abstract which has been sent to us by "Russia To-day" Press Service, the Editor of which is Mrs. R. Townsend, may have a bearing on practical problems, *e.g.*, motor driving, flying, etc.

ABSTRACTS

I.—CONJUNCTIVA

(1) **Luo, T. H. (Peking).—Conjunctival lesions in tuberous sclerosis.** *Amer. Jl. of Ophthal.* Vol. XXIII, p. 1029, 1940.

(1) **Luo** describes the case of a Chinese woman, aged 37 years, who was suffering from tuberous sclerosis. The palpebral conjunctiva of both lower lids and the left upper lid margin exhibited a

number of slightly raised, pedunculated, greyish white neoplasms about 4 mm. in diameter, their surface being smooth and flat. Histological examinations of these neoplasms showed masses of collagenous connective tissue, covered by several layers of epithelial cells, and in some places containing tubules or cords of epithelial cells and pseudo-glandular structures. With Verhoeff's elastic tissue stain it was evident that there were no elastic fibres.

In the upper nasal quadrant of the left fundus there was a white oval patch, the nature of which was uncertain. The author comments on the variety of tuberous sclerosis lesions.

H. B. STALLARD.

(2) **Sindermann, H. R. (Toronto).—External ophthalmoplegia. A case of myasthenia gravis.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 1035, 1940.

(2) **Sindermann** comments that ptosis or diplopia may be the earliest symptoms in cases of myasthenia gravis and on this account patients first consult the ophthalmologist. He quotes Uhthoff who found ptosis as the first symptom in over 50 per cent. of myasthenia gravis cases and absent in only 18 per cent. of all cases; and the extra-ocular muscles involved in 30 per cent.

The author describes the case of a young male, aged 27 years, in whom the diagnosis became evident on using a hypodermic injection of 3 c.c. of prostigmin 1/4,000 and atropine sulphate 1/200 as a therapeutic test. The inter-palpebral aperture was measured before the test, at 10 minutes and 1 hour after injection, and the action of the extra-ocular muscles noted at these times.

H. B. STALLARD.

(3) **Braley, Alson (Detroit).—Intra-cellular bodies of the conjunctival epithelial cells.** *Arch. of Ophthal.*, October, 1940.

(3) **Braley's** report is written with a view to clearing up the confusion at present existing with regard to the various types of inclusion bodies found in scrapings of the conjunctival epithelium. In addition to those in trachoma and inclusion blenorrhoea, intracellular bodies may be derived from mitochondria, pigment, keratin, mucin from goblet cells, nuclear extrusions, phagocytosed cellular debris, and extracellular bacteria. If, therefore, microscopical diagnosis of trachoma and inclusion blenorrhoea is to be placed on a firm basis, differential diagnosis of the various types of inclusion bodies is essential. Scrapings should be taken from the conjunctivae of the upper and lower lids by a platinum wire spatula, after removal of surface discharge. Giemsa's stain is the more reliable, but for quick results Wright's stain is recommended. Inclusion bodies in trachoma and inclusion conjunctivitis are of two types. The

elementary body is an intracytoplasmic mass composed of uniformly sized purple staining granules in a relatively clear matrix, the latter being composed of a glycogen-like substance which stains a deep golden brown with iodine. The initial body is composed of one or more large blue staining bodies in the cytoplasm of the conjunctival epithelial cell. It is usually round or oval and about the size of a streptococcus. In most cases, trachoma is indicated, if scrapings from the upper lid show typical inclusions while those from the lower lid show few or none, the reverse being the case in inclusion conjunctivitis. Some of the points in differential diagnosis are these:—Mitochondria granules have a diffuse irregular appearance and are quickly unstained by alcohol, while elementary bodies are alcohol fast. Particles allied to keratin which develop in old cultures especially in the presence of a chronic irritant, may be differentiated on the bases of their red colour and the marked variation in size of the particles. Goblet cells may show homogeneous blue staining masses in their cytoplasm, but these are not alcohol fast. Melanin granules can be diagnosed by their colour in unstained specimens. Extrusions of nuclear material are identified by being composed of chromatin. Phagocytosed cellular debris is often present, particularly in trachoma, and can be diagnosed by its staining a uniform dark blue colour.

In a discussion on Braley's paper, Philip Thygeson mentioned that other inclusion bodies can be found on rare occasions in conjunctival cells, *e.g.*, in cases of herpes zoster, varicella, variola, and especially in lymphogranuloma venereum. He also emphasised the presence of free inclusion body components, as an aid to diagnosis.

F. A. W-N.

II.—TRACHOMA

(1) **Julianelle, L. A. (Saint Louis).—The infectivity of trachoma. X. Frequency and distribution of the inclusion body and its possible relation to pathogenesis.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 633, 1940.

(1) **Julianelle** examined 602 patients in different stages of trachoma, for inclusion bodies, which he found in approximately 1 in 3 cases. In the first six months of the disease these bodies may be evident in half the patients, from then on their incidence falling gradually to zero at about ten years duration.

Inclusion bodies are also found in the epithelial cells of swimming bath conjunctivitis and inclusion blenorrhoea, but the differentiation

of these disorders from trachoma rests on the important clinical fact that the onset of the former is acute and sometimes explosive, whereas the latter begins insidiously. However, the presence of inclusion bodies is of diagnostic value in trachoma for their incidence is highest in the early stages of the disease when the clinical features are not so clear cut as they are at later stages, in which the inclusion bodies are often absent.

From experiments on monkeys it would seem that the inclusion body may be a factor in the pathogenesis of trachoma for tissues with inclusion bodies have twice the capacity to cause infection than those without. The author states that his experiments yield data which suggest that inclusion bodies may be a mass of virus particles, although the evidence for this is not yet conclusive. The clinical implication in this conception is that as a patient loses inclusions he ceases to be a source for disseminating trachoma.

The author found that in certain instances inclusions were present in one eye only despite clinical activity in both, but in genuine monocular trachoma inclusion bodies were associated only with the infected eye.

Inclusion bodies are the first sign of infection in the fellow eye when the disease has actually begun in the other eye. The inclusion bodies precede conjunctival thickening or follicular formation.

In recurrent trachoma inclusion bodies appeared in approximately the same frequency as trachoma of recent onset.

H. B. STALLARD.

(2) **Bengston, Ida A. (Washington).—The question of the Rickettsiae nature of trachoma.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 770, 1940.

(2) **Bengston** reviews the literature and the experimental work concerning the presence of inclusion bodies of Halberstaedter-Prowaczek and Rickettsiae; the louse transmission of the trachoma virus, and the Weil-Felix reaction in the diagnosis of trachoma.

She carried out experiments to ascertain (1) the morphology and distribution in the cell of true Rickettsiae and the elementary bodies of trachoma (2) the significance and value of the Weil-Felix test and (3) agglutination tests using as antigens suspensions of the organisms of three Rickettsiae diseases, endemic typhus, the " Q " fever of Australia, and nine mile fever.

The author was able to obtain material rich in Rickettsiae by the method of differential centrifugation and protein precipitations, and in Maitland media cultures. The Rickettsiae are typically bacillary; very small coccoidal and irregular-shaped forms occur; they are also pleomorphic, particularly in the cells of arthropods.

The inclusion body in the early stages of trachoma consists of

elongated rod-shaped organisms (initial bodies of Lindner), indefinite in outline and staining bluish with Giemsa. Later these bodies appear to coalesce, become less dense and form the bluish matrix in which the small coccoidal elementary bodies are embedded.

The elementary bodies appear to be the typical form of the organism, they are round and uniform in size though small, their evolution is described as a developmental cycle.

The results of the Weil-Felix test showed that it would not be of any diagnostic value and that in early diagnosis of trachoma it would be of less significance than the clinical signs. Agglutination tests carried out against three antigens (1) the Wilmington strain of endemic typhus (2) Burnet's "Q" fever strain and (3) the X-strain of nine mile fever showed no agglutination and therefore no evidence of antigenic relationship.

The author has tentatively defined Rickettsiae as small intracellular bodies, requiring Giemsa stain for their demonstration, an arthropod host and failing to grow on artificial media.

H. B. STALLARD.

(3) **Harley, R. D., Brown, A. E. and Herrell, W. E. (Rochester, Minnesota).—Sulphanilamide and neoprontosil in the treatment of trachoma.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 662, 1940.

(3) **Harley, Brown and Herrell** review the literature about the treatment of trachoma with sulphanilamide. They comment on the work of Bellows and Chinn (*Jl. Amer. Med. Assoc.*, CXII, 2023, 1939), who detected sulphanilamide in all ocular tissue within 15 minutes of its oral administration and found the maximum concentration of the drug about the sixth hour. Mention is also made of the 12 children affected by this disease who were treated by Richards, Forster and Thygeson (*Arch. of Ophthal.* XXI, 577, 1939), in whom disappearance of the trachoma was judged by the disappearance of inclusion bodies during treatment and the failure of pooled epithelial scrapings, taken on the 29th day, to infect baboons.

In the author's series of 11 cases of trachoma in stages II and III, neoprontosil was given orally. It has a lower toxicity and is better tolerated than other sulphanilamide preparations and lends itself well to the treatment of chronic conditions in which prolonged therapy is necessary. Six patients received sulphanilamide only, three began with sulphanilamide but because of its toxic effects this was changed for neoprontosil, and the latter drug was used exclusively in one case.

The results of neoprontosil treatment are neither so dramatic nor so rapid as those produced by sulphanilamide, but prolonged

treatment of trachoma by neoprontosil compares favourably with the results of sulphanilamide treatment.

In the 11 cases objective and subjective improvement occurred in all; four were intolerant to sulphanilamide, three of which continued with neoprontosil and showed good results.

H. B. STALLARD.

(+) **Thygeson, P. (New York).—The treatment of trachoma with sulphanilamide.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 679, 1940.

(4) **Thygeson** treated 31 cases of trachoma, representative of all stages and complications of the disease, with sulphanilamide. Six of these patients had never received any form of therapy. Whenever possible they were hospitalized for 10-14 days and the dose of sulphanilamide was sufficient to give a blood concentration of 5 mg. per ml. or higher. Those receiving out-patient treatment had lower dosages, 30-40 grains a day in equally divided doses, given with equal amounts of sodium bicarbonate, continued over 5-8 weeks. In 16 cases there was apparent healing without recurrence, both early and late cases treated with high and low doses, 11 were improved and 4 unimproved.

Sulphanilamide therapy was particularly dramatic in cases with severe corneal symptoms, photophobia sometimes disappearing in 24 hours, ulceration and filtration healing in the first week. After 13 days of treatment all photophobia disappeared, the bulbar conjunctiva became white, the pannus vessels were no longer dilated and the subepithelial infiltration and epithelial changes disappeared. In three acute cases conjunctival discharge ceased at once and papillary hypertrophy disappeared. Relatively avascular follicular lymphoid tissue is absorbed much more slowly and may continue to be so long after the administration of the drug has ceased.

In all the 11 improved cases some degree of conjunctival inflammation persisted, but only one of these cases received the full doses, the remainder being treated in out-patients on low doses.

The four unimproved cases included none that was early and none in which epithelial cell inclusions had been found. All were in the cicatricial stage.

Sulphanilamide therapy had little effect on cases of secondary infection with haemophilus influenzae, diplococcus pneumoniae and staphylococcus aureus and no effect in two cases complicated by dacryocystitis.

Sixteen cases showed inclusion bodies which were numerous in the acute cases and relatively scarce in the chronic. Sulphanilamide caused the rapid disappearance of these and in no case were they found after the third day. Before disappearing their staining reactions with Giemsa became poor and the elementary and initial

bodies presented a fuzzy appearance. Ten of the sixteen cases showing inclusion bodies were healed.

The results are in favour of a full therapeutic dose over a period of two weeks or a little longer.

H. B. STALLARD.

III.—MEDICAL OPHTHALMOLOGY

(1) **Hagedoorn, A. (Amsterdam).—Amaurotic idiocy and related conditions.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 735, 1940.

(1) **Hagedoorn** discusses the pathology of amaurotic idiocy and lipoidosis and classifies amaurotic idiocy as infantile, juvenile and adult. He comments that the chemical knowledge of these disorders is very incomplete, and that each family has its own peculiar characteristics in the nature and physical properties of the lipoidosis. In infantile amaurotic idiocy the cytoplasm of the retinal ganglion cells is swollen, stains pink or pale orange with Sudan III and the lipoid granules stain with the haematoxylin-lac method. In the juvenile and adult cases both ganglion cells and mesodermal cells are affected, and the deeper layers of the retina are also involved.

He describes bio-chemical experiments on animals in which lecithin, cephalin and sphingomyelin were adminisrered parenterally, subcutaneously and intravenously and the blood, its cells and the tissues of the reticulo-endothelial system searched for the presence of these chemical substances.

It seems from these experiments that the normal ganglion cell is unaffected by lipoidemia and so in amaurotic idiocy there probably exists a defective metabolism of the ganglion cells. It would appear, at present impossible to differentiate between infantile amaurotic idiocy and Neimann-Pick's disease on the morphological characters and the colour tests for the lipoid granules and their chemistry. In the case of infantile amaurotic idiocy described by the author, foam cells were found in the spleen and heart. The quantity of lecithin in the blood increased during the last few weeks of life. Sections of the retina were stained with Sudan III, the cytoplasm of the affected cells in the ganglion cell layer stained pale orange, and the nerve fibre layer was reduced in size. Degenerative changes were particularly well marked in the temporal half of the optic nerve prepared with specific medullary-sheath stain.

The numbers of ganglion cells were judged to be less than normal and glial cells filled with lipoid material.

Changes were also seen in the amacrine cells, and the author comments that the presence of lipophages in the sheath of the optic

nerve suggested that the processes in the brain were more advanced than in the retina and points to an abnormal lipoid content of the cerebro-spinal fluid at the time of death. Before death the blood showed a raised lipoid content, probably as a result of degeneration of the brain.

This paper is illustrated by thirteen good microphotographs and there is an extensive bibliography. As a discourse it is loosely knit together, rambling and lacks lucidity and conciseness in assembling all the available clinical and experimental facts and discussing their pathological significance.

H. B. STALLARD.

(2) **Lewis, P. M. (Memphis, Tennessee).—Ocular complications of meningococcic meningitis.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 617, 1940.

(2) **Lewis** comments that ocular complications of meningococcic meningitis are more frequent when an epidemic is at its peak. About 44 per cent. in his series of 350 cases showed some ocular abnormality. Simple engorgement of the retinal veins accounted for 14 per cent.; papillitis 12 per cent. and hyperaemia of the optic disc and retina 11·4 per cent.

Retraction of the eyelids so that the sclera above and below the cornea is visible, diminished winking and staring, have been noted in the literature. Conjunctivitis is present in some cases the source of infection being endogenous or a direct spread from the nose and mouth, it clears up in one to five days with appropriate treatment.

Very rarely subconjunctival haemorrhage occurs. Keratitis, ulcerative and parenchymatous, is evident in some cases.

Authorities vary in their statements as to the incidence of strabismus from 2·43 per cent. to 31·2 per cent. of cases. The author found it in 4·28 per cent. It is usually paralytic and the VI nerve is most frequently affected. The prognosis is good. He quotes Parsons who found kinetic strabismus or conjugate lateral deviation of the eyes in the early stages of the disease, due to lesions in the cortex or in the pons. Cranial nerves other than the VI may be involved and the paralysis be complete or partial. Total palsy of the III and IV nerves is rare, sometimes the V is involved and loss of corneal anaesthesia and neuroparalytic keratitis result.

Nystagmus is rarely seen. The frequency of pupil abnormalities such as mydriasis, anisocoria, miosis, hippus and deficient reflexes varies.

Endophthalmitis occurred in 19 out of the author's 350 cases, and in four of these the condition was bilateral. It is endogenous. This complication is more frequent among children. There seems to be no relationship between the severity of meningitis and the occurrence of endophthalmitis. It manifests itself early in the disease, the earliest being the second day, and the latest the 12th.

The incidence of death is rather lower in patients suffering from this complication than in those in whom it is absent. Meningococci have been identified inside the eye, by culture from a hypopyon and by histological examination of the intra-ocular tissues.

The author describes two cases of endophthalmitis which ended in destruction of the eye in spite of aspiration of the anterior chamber and intra-ocular and subconjunctival injection of anti-meningococcal anti-toxin.

Optic neuritis, generally bilateral but often more marked on one side, was present in 12 per cent. of the 350 cases. This figure agrees approximately with a number of authors' findings. Papilloedema is rarer and occurred in only three cases in this series. Optic neuritis occurs early in the course of the disease and reaches its height about the 2nd or 3rd week. Partial optic atrophy appears later.

Amaurosis with normal pupil reactions is due to involvement of the higher centres. In one case reported in the literature a binasal field defect and partial optic atrophy suggested a lesion in the chiasma.

Central retinal vein thrombosis has been rarely seen and generally occurs in association with vascular sclerosis. The author reports a case of thrombosis in both central retinal vessels in a patient suffering from metastatic endophthalmitis.

In discussing the general treatment of meningococcal meningitis, the author discusses the value of intravenous anti-meningococcal anti-toxin, 100,000 units intravenously as the initial dose; sulphanilamide 100 grains orally followed by 20 grains four-hourly; lumbar puncture and subtemporal decompression in cases where the degree of papilloedema is considered dangerous.

H. B. STALLARD.

(3) **McGregor, H. G. (Brighton). — Exophthalmic ophthalmoplegia.** *Lancet*, Vol. II, p. 579, 1940.

(3) **McGregor** records the case of a man aged 37 years, in whom ophthalmoplegia was present for three months before the onset of severe exophthalmos. He comments that this tends to disprove the idea that the ophthalmoplegia is the result of a rapidly produced exophthalmos. The onset of this disorder is usually subacute and the paralysis is not of individual ocular muscles, but of movements of the eye in a particular plane.

Paralysis limited to the ocular muscles, the absence of fatiguability and no response to prostigmine are clinical features which differentiate exophthalmic ophthalmoplegia from myasthenia gravis complicating thyrotoxicosis.

The rôle of the thyrotropic hormone of the pituitary in the production of exophthalmos is discussed.

H. B. STALLARD.

(4) **Jackson, E.—Undulant fever and the eye.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 824, 1940.

(4) **Jackson** remarks that in undulant fever the eye lesions may be the first positive evidence of nervous system disturbance. The ocular lesions recorded in the literature are a phlyctenular disorder of the conjunctiva and cornea; hypopyon; iritis; panophthalmitis; choroido-retinitis; retinal vascular congestion and haemorrhages; optic neuritis; papillitis; papilloedema; extra-ocular muscle palsy, particularly abducens palsy; dilated and fixed pupils and restricted visual fields.

H. B. STALLARD.

IV.—MISCELLANEOUS

(1) **Verhoeff, F. H. (Boston), and Simpson, G. Victor (Washington, D. C.).—Tubercle within central retinal vein.** *Arch. of Ophthal.*, October, 1940.

(1) **Verhoeff** and **Simpson's** case was first seen at the age of 31 years in 1931, when he complained of defective vision in the right eye, which was found to be due to haemorrhage into the vitreous. The left eye was unaffected, and under tuberculin, the haemorrhage in the right gradually absorbed. Clinically and radiologically the chest was normal. Two years later an enlarged inguinal gland was removed and sections showed chronic inflammatory changes. In May, 1934, the left eye failed and examination showed thrombosis of the central retinal vein. This was followed a few days later by secondary glaucoma, which necessitated removal of the eye. At this time, the right eye was still unaffected and had no recurrence of haemorrhage. Pathological examination of the left eye showed numerous retinal haemorrhages, a vascularised membrane over the disc extending to the macula, and some other evidence of retinitis proliferans. Serial sections of the disc and optic nerve showed cupping and the presence of connective tissue rich in new vessels and capillaries. The central artery was unaffected, but the lumen of the vein about 1 mm. behind the lamina was found to be occupied by a growth of epithelioid cells, without any giant cells, the surrounding tissues being infiltrated with lymphocytes. Five other tubercles were found in relation with the optic nerve. No tubercle bacilli were found in the mass within the central vein, but the histological changes were sufficiently characteristic to confirm the diagnosis. The only similar case in the literature was one of Safar's, where a tubercle was found within the central retinal vein just behind the lamina, and again no tubercle bacilli were found. The authors are of opinion that although only one case other than their

own has been reported, the condition of partial or complete tuberculous obstruction of the central vein is a frequent cause of suddenly occurring extensive retinal haemorrhages in young persons.

F. A. W-N.

(2) **Kronfeld, P. C. (Chicago).—A note on the treatment of the sequelae of perforated corneal ulcer.** *Amer. Jl. of Ophthal.*, Vol. XXIII, p. 1014, 1940.

(2) **Kronfeld** describes his experiences in the treatment of perforated corneal ulcers at the Peking Union Medical College, where two-thirds of all intra-ocular operations are performed for the correction of these complications. He comments that there is a direct relationship between the extent of the anterior synechiae developing during the healing of a perforated corneal ulcer and the incidence and severity of secondary glaucoma.

In cases of iris prolapse he pulls on the prolapse so as to induce irido-dialysis and then excises the entire dialysed sector. As regards conjunctival flaps, the author has noted that restoration of the anterior chamber after closure of the corneal wound with a bridge flap takes considerably longer than after closure with an apron flap.

For secondary glaucoma due to adherent leucoma, a combination of cyclodialysis with total iridectomy in the same sector of the globe and at the same time, is reported as being most effective.

Corneal fistulae are commonly at or near the centre of the cornea where the pupil border has prolapsed. They are sometimes a safety valve in maintaining normal intra-ocular pressure and on this account closure is sometimes difficult and if achieved may lead to glaucoma. A two stage operation is recommended (1) combined cyclodialysis and iridectomy (2) excision and replacement of the fistula by corneal transplantation.

Staphylomata were treated by a preliminary cyclodialysis with iridectomy followed later by partial elliptical excision of the staphyloma between corneal sutures. In children anterior staphylomata were treated by repeated multiple cauterizations of the wall of the staphyloma with a high frequency current.

The site for optical iridectomy was selected by testing the visual acuity five minutes after subconjunctival injection of adrenalin made at three or four different sites on consecutive days. The author comments that any type of incision in or near the limbus adds to the corneal opacity of the corresponding sector. He prefers to make an incision to the side of the chosen sector for iridectomy and to perform the difficult task of making an elliptical iridectomy with iris forceps and de Wecker's scissors passed into the anterior chamber beneath the selected part of the cornea.

H. B. STALLARD.

CORRESPONDENCE

MUSTARD GAS AND ITS IMPLICATIONS

To the Editors of THE BRITISH JOURNAL OF OPHTHALMOLOGY.

DEAR SIRS,—In reply to Messrs. John Eyre and Frank W. Law may I state that I have seen one drop of 4 per cent. solution of hyd. perchlor. in glycerine accidentally fall on the cornea and in a few seconds which elapsed before washing out the conjunctival sac, severe and lengthy, but not permanent damage was inflicted on almost the whole of the corneal epithelium. Here there was no question of absorption. I quite agree with them that in the field of biology there is nothing more misleading than the argument from analogy, which indeed led eminent men to assume and publish results on the assumption that because man could accommodate the mammals could also.

But the argument from analogy hardly applies in this instance just quoted.

As regards the late effects of mustard gas on the cornea, the few cases I have seen showed deep seated infiltration rather than ulceration and there was very little clear cornea left anywhere. So that I doubt whether either diathermy or contact glasses would have assisted. If such cases, which I am glad to say are rare, present themselves, the method suggested will be borne in mind. It is true that these conditions do recur without obvious cause. No one will be more grateful than myself if the writers have devised an effective treatment of mustard gas in the field, and will look forward to their publication of their experimental results. But the practical use of any remedy of the kind in advanced positions of any army is very difficult but not insuperable.

Some idea of the difficulty of acting efficiently in advanced stations may be learnt from the Palestine campaign, where towards the end men with high temperature were given quinine at once, no matter what seemed to be the cause of the temperature. If the medical officers had waited until they could be sure that malaria was the cause it would at times have been too late. To neutralise the effects of mustard on the eyes, special instruction for the forward units will be a necessity.

I am, etc.,

JAMES W. BARRETT.

MELBOURNE,
October 14, 1940.

NOTES

Death

WE regret to record the death of William Wallace, the well-known composer and writer on musical subjects, on December 16, 1940. Wallace received his education at Fettes and the University of Glasgow; he qualified M.B., C.M. in 1885 and took the M.D. (with commendation) three years later. During the Great War Wallace was appointed ophthalmologist to the Colchester Military Hospital and later served as Captain, R.A.M.C., attached as eye specialist to the London district. He had, early in his career, been house surgeon for two years at the Glasgow Eye Infirmary and clinical assistant at Moorfields Hospital.

He recorded his ophthalmic experiences in the war years in our third volume (1919) p. 481. In the same volume he wrote on the beginnings of fundus illustration, p. 102. The early ophthalmoscopic atlases was a subject to which he had devoted much attention, and the writer remembers Wallace showing him some of his books about this time. He was especially proud of his copy of Bannister. But it is as a musician that he will chiefly be remembered. For years he was secretary to the Philharmonic Society and he was the author of "The Threshold of Music" as well as works on Wagner and other musical subjects. A series of his drawings in water colour of eye injuries is in the Army Medical War Museum.

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Shares in the British Journal of Ophthalmology

A SMALL number of shares in the Company owning the British Journal of Ophthalmology occasionally come into the market as members die. At present there are shares to be had. It is hoped that the younger members of the ophthalmic circle will apply for them. Applications should be addressed to the Managing Director, c/o the Manager, 24, Thayer Street, London, W.1.

FUTURE ARRANGEMENTS

1941

February 1, 1941.—North of England Ophthalmological Society, at Newcastle-on-Tyne.

March 1, 1941.—North of England Ophthalmological Society, at Liverpool.

March 29, 1941.—North of England Ophthalmological Society, at Sheffield.